Medical Literature

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Outline

- Study design
- Statistical methods
- Risk measurements
- Statistical tests

Learning Objectives

- 1. To list and define study designs and their advantages/disadvantages
- 2. To define, calculate and interpret sensitivity and specificity as characteristics of a test
- 3. To define, calculate and interpret measures of risk including RRR, ARR, OR
- 4. To define applications for chi-square test, sample and student T tests; to interpret p values

Study design

- N of 1
- Randomized Control Trial
- Cohort Study
- Cross Sectional Survey
- Case-control Study
- Case Report and Case Series

N-of-1 Trials

Experimental design in which alternative treatments for a chronically affected individual are administered in a random sequence and the individual is observed in a double blind fashion to determine which treatment is the best.

Advantages:

- Best study for individual patient
- Blinding

Disadvantages:

- Cost, time

Randomized Control Trial

Individuals similar at the beginning are randomly allocated to two or m
Outcomes from each groups are compared after sufficient follow-up tim

Advantages:

- unbiased distribution of confounders
- blinding more likely
- randomization facilitates statistical analysis

Disadvantages:

- expensive: time and money
- volunteer bias
- ethically problematic at times

Cohort Study

Prospective, observational study over time of a group that is initially disease free with some of the group having the potential of being exposed to the exposure of interest, in order to determine the association between that exposure and an outcome.

<u>Advantages</u>:

- ethically safe
- subjects matched;
- can establish timing and directionality of events;
- eligibility criteria and outcome assessments can be standardized
- easier and cheaper than RCT

<u>Disadvantages</u>:

- controls may be difficult to identify
- exposure may be linked to a hidden confounder
- blinding difficult
- randomization not present
- for rare disease, large sample or long follow-up necessary

Cross-Sectional Survey

A descriptive observational study of the relationship between diseases and other factors at one point in time (usually) in a defined population.

Advantages:

- cheap and simple
- ethically safe

Disadvantages:

- establishes association at most, not causality
- recall bias susceptibility
- confounders may be unequally distributed
- Neyman bias
- group sizes may be unequal

Case-Control Studies

Retrospective, observational study often based on secondary data in which the proportion of cases with a potential risk factor are compared to the proportion of controls (individuals without the disease) with the same risk factor.

<u>Advantages</u>:

- quick and cheap;
- only feasible method for very rare disorders or long lag time;
- fewer subjects needed.

<u>Disadvantages</u>:

- reliance on recall or records to determine exposure status;
- confounders;
- selection of control groups is difficult;

Case report/case series

An observational study of a case or series of cases, typically describing the manifestations, clinical course, and prognosis of a condition.

Advantages:

- Relatively inexpensive
- Short time course

Disadvantages:

- Anecdotal
- No statistical testing can be applied

Statistical methods

- Sensitivity
- Specificity
- Positive Predictive Value
- Negative Predictive Value

Sensitivity and Specificity

- **Sensitivity** is the proportion of people with disease who have a positive test.
  - **SnOUT: sensitivity rules out disease**
- **Specificity** is the proportion of people free of a disease who have a negative test.
  - **SpIN: specificity rules in disease**

Sensitivity and Specificity

Test \ Disease	Yes	No
Yes	**TP**	**FP**
No	**FN**	**TN**

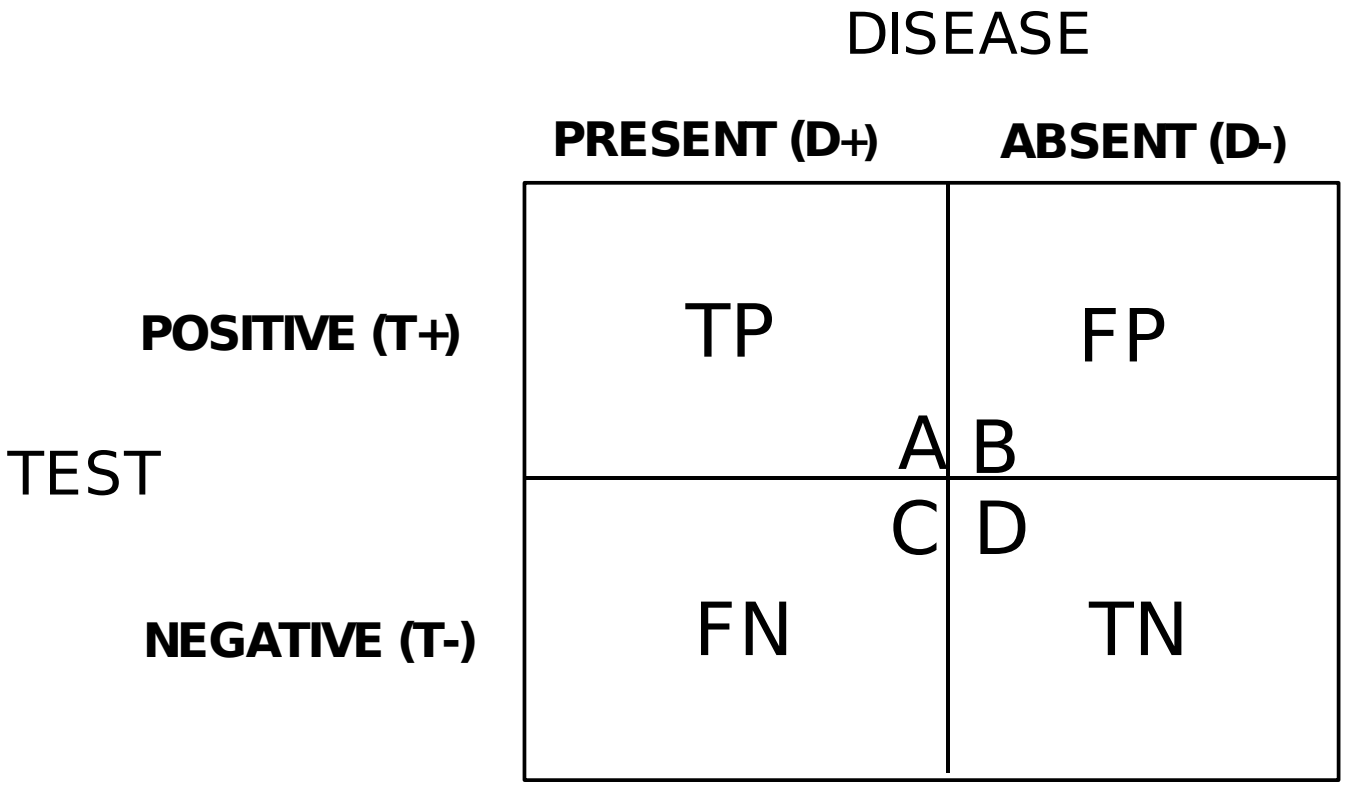
Sensitivity= TP/TP+FN

Specificity=TN/TN+FP

Positive predictive value=TP/TP+FP

Negative predictive value=TN/TN+FN

Sensitivity and Specificity



Example:
Calculate sensitivity, specificity, PPV, and NPV of this new thyroid cancer test.

A colleague has told you that there is a new blood test for diagnosing thyroid cancer. Before you decide if you want to use it in your clinic, you look at one of the published studies. In the study,there were a total of 2300 enrolled patients. All of these patients had the new blood test and a subsequent thyroid biopsy.

There were 463 people who had positive blood test results, but only 215 of these people who tested positive actually had thyroid cancer on biopsy.

There were 1837 people who had negative test results, and 1822 of these people actually had negative biopsy results.

Sensitivity and Specificity

Test	Disease=**Thyroid CA** Yes	No	
Pos	**215**		**463**
Neg		**1822**	**1837**
			2300

Sensitivity=TP/TP+FN

Specificity= TN/TN+FP

PPV= TP/TP+FP

NPV= TN/TN+FN

Sensitivity and Specificity

Test	Disease=Thyroid CA: Yes	Disease=Thyroid CA: No	
Pos	215	248	463
Neg	15	1822	1837
	230	2070	2300

Sensitivity=215/(215+15)=93%

Specificity=1822/(1822+248)=88%

PPV=215/(215+248)=

NPV=1822/(1822+15)=99%

Risk measurements

- Absolute Risk Reduction
- Risk Ratio
- Relative Risk Reduction
- Odds Ratio
- Number Needed to Treat

Absolute Risk Reduction (ARR)

- difference in the event rate between control group (CER) and treated group (EER)

- **ARR = CER - EER.**

The ABSOLUTE arithmetic difference in rates of bad outcomes b/w the untreated and treated groups

Example:
Calculate the absolute risk reduction of Aspirin in patients with coronary heart disease.

You performed a study of ASA in patients with CAD. You have 130 pts with CAD in your study. 65 of those pts are treated with ASA for one year.

You found that, in the untreated group, 50/65 (77%) had an MI.

In the treated group, only 5/65 (8%) had an MI.

Absolute risk reduction

Treatment=Aspirin	Disease=MI: Yes	Disease=MI: No	
Yes	5	60	65
No	50	15	65
			130

ARR = CER - EER.

ARR= 50/65 – 5/65= .77 - .08= .69

Risk Ratio

- RR is ratio of risk in the treated group (EER) to the risk in the control group (CER): **RR=EER/CER**.
- Relative Risk Reduction (RRR) is the percent reduction in events in the treated group event rate (EER) compared to the control group event rate (CER):

RRR = (CER - EER) / CER * 100

PROPORTIONAL reduction in rates of bad outcomes b/w the untreated and treated groups used in randomized trials and cohort studies.

Relative risk reduction

Treatment =ASA	Disease= MI: Yes	Disease= MI: No	
Yes	5	60	65
No	50	15	65

RR = EER/CER.
RR= (5/65)/ (50/65)=.08/.77=.

RRR = (CER - EER) / CER x 100

RRR= (50/65 – 5/65)/

Odds Ratio

- **Odds** are a ratio of events to non-events.
- **Odds** of an experimental patient suffering an adverse event relative to a control patient.
- If the event rate for a disease is 0.1 (10%), its nonevent rate is 0.9 and therefore its odds are 1:9, or 0.111.
- Used in case control studies

Example:
Calculate the odds ratio for getting lung cancer if you are a smoker (compared to non-smoker).

Exposure is smoking and disease is lung cancer.

Let’s start with 100 people with lung cancer and 100 people without lung cancer and then look back to see who smoked. (case control design)

Of the 100 people with lung cancer, 90 of those people smoked and 10 did not smoke.

Of the 100 people without lung cancer, 40 of those people smoked and 60 of those people did not smoke.

Odds ratio

Exposure=Smoking	Disease=Lung CA: Yes/case	Disease=Lung CA: No/control=
Yes	**90**	**40**
No	**10**	**60**
	100	100

OR= (a/b)/(c/d)=(90/40)/(10/60)=13.5

Number Needed to Treat (NNT)

- number of patients who need to be treated to prevent one bad outcome.

- the inverse of the ARR:

NNT = 1/ARR

Number needed to treat

Treatment=ASA	Disease=MI: Yes	Disease=MI: No
Yes	5	60
No	50	15

ARR = CER - EER.
ARR= 50/65 – 5/65=.69

NNT=1/ARR
NNT=1/.69=1.4

Statistical analysis methods

- Central tendency
- P value
- Chi-Square Test
- T test

Central tendencies

Median: Value that exactly one-half of the values are less than and one-half of the values are more than when the values are sorted in numerical order.

Mean: Average value of a data set and mathematically is the sum of all values divided by the number of values.

Mode: Most common data value, which is the highest peak of a frequency distribution.

P value

Probability that an outcome as large as or larger than that the outcom chance variability of individuals or measurements alone.

- If Null hypothesis states that the means of two groups are equal, then the P value states that there is an X% chance that this difference seen in the study is due to chance.
- P<.05 statistically significant- 5% chance that this difference was found by chance alone.

Chi-Square Test

- tests the **null hypothesis,** which states that there is no significant difference between the expected and observed result
- compares observed data with data we would expect to obtain according to a specific hypothesis
- ??????????????????????????

Chi Square

- chi-square is the sum of the squared difference between observed (o) and the expected (e) data (or the deviation, d), divided by the expected data in all possible categories

T-tests

- Sample T test: assesses whether the means of two groups are *statistically* different from each other (no assumptions of distribution)
- Student T test: same but assumes a Gaussian distribution
- Paired Student T test: assesses whether means of same group tested in different points in time are different from one another

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